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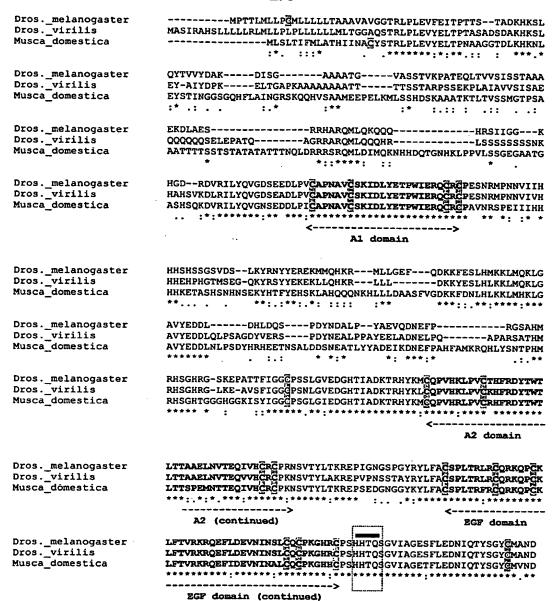
Drosophila	C. elegans	D. Melanogasta D. Melanogasta D. Melanogasta D. Melanogasta	Homo sapiens Homo sapiens Homo sapiens Homo sapiens Homo sapiens	Homo sapiens Homo sapiens Homo sapiens Homo sapiens Homo sapiens Mus muscilus	
<u>—</u> ĞH <u>RĞ</u> PSHHTQSG-	ĒTRĒDRHYVQAF-	GNEGENKWPDSR- GERCAYKSWNGD- GORCEYKEIDNT- GERGEYKEIDGS-	GARGIENVPMKV- GORGLEKLPLRL- GORGLEKLPLRL- GORGOFAMVNF- GORGOOFLPKTD	GERCOYRDLKWW- CARCEHADLLAV- CARCERVDLFYL- GERCGEKSMKTH- GERCGEKSMKTH- GERCHGLSLPVE- GYRGEHFELTVH- GYRGEHFELTVH-	<u>(</u>
FAĞSP-LTRLRĞQRKQPĞKLFTVRKRQEFLDEVNINSL <u>@</u> QĞPK	IEKLKEAKĞKDYĞHHNATĞHVEVIFREDRVSAVVPSĞHÜPQGWEĞTRĞDRHYVQAF-	EVYŒŒŒPTEYEĞNKWPDSR- TVFHS@LĞVNDYDĞERÇAYKSWNGD- PVYS-ŒĞAIGENĞORĞEYKEIDNT- ILYN-ŒŒĞALGENĞPRĞEYKEIDGS-	NPSRYLÖKÖOPGFTGARGIENVPMKVNPSRYLCKÖPNEFTGARGONYWASFOLSCKÖPNGFRGORGIEKLPLRLOLSCKÖPVGYTGDRGORGURDO-FLPKTDSHKHCRGKGKGYOGVRGDO-FLPKTDSPFCRCVENYTGARGEVELPGS-	KYAĞNĞVYGYIĞERĞQYRDLKWWKPAĞVÇHSGYVĞARĞEHADLLAVTPSĞVĞDEGYIĞARĞERVDLFYLAVTĞRĞQEYRĞERĞHGLSLPVEQNYĞRĞEVGYTĞQRĞEHFFLTVHQNYĞRĞFTGYTĞQRĞEHFFLTVHQAIĞRĞFTGYTĞQRĞEHFFLTVHQAIĞRĞFTGYTĞQRĞEHFFLTVHQAIĞRĞFTGYTĞQRĞEHFFLTVHQAIĞRĞFTGYTĞQRĞEHFFLTVHQAIĞRĞFTGYTĞQRĞEHFFLTVH	ඟ න
Ğorkopğkletvrkroe	Ğhhnatğhvevi fred-	lipönfdyöfhngtörmipdin Ilpöseayntsfölngghörqhpwnn yköpetfdawyölndahöfavkiadl fağpptyvawyölndctöftvkihne	VKČAEKEKT-FÖVNGGEÖFMVKDLS VKÇAEKEKT-FÖVNGGEÖFMVKDLS NRKÖNETAKS-YÖVNGGVÖYYIEGIN NRKÖNETAKS-YÖVNGGVÖYYIEGIN NRKÖNETAKS-YÖVNGGVÖYYIEGIN NRKÖNETAKS-YÖUNGGVÖYYIEGIN NRPÖRDKDLA-YÖLNDGEÖFVIETLTG NRPÖRPKNS-FÖLNGGLÖGYIETITG	SEĞPLSHDG-YĞLHDGVÖMYIEALD NDCPDSHTQ-FÖFH-GTÖRFLVQED SROPKQYKH-YÖIK-GRÖRFTVVAEQ NPĞNAEFQN-FÖIH-GEĞKYIEHLE NDPĞLRKYKD-FÖIH-GEĞKYKEIR TRĞSSDMNG-YÖLH-GOĞIYLVDMS HPĞLEDHNS-YÖIN-GAĞAFHHELK	(©)
PGYRYLFAĞSP-LTRLR	IEKLKEAKĞKDY	DRSASGIPĞNFDYĞFHNGTĞRMIPDIN ETEIQMLPĞSEAYNTSFĞLNGGHĞFQHPMVNN- NITFPTYKĞPETFDAWYĞLNDAHĞFAVKIADL- NVTFPIFAĞPPTYVAWYĞLNDGTĞFTVKIHNE-	TGTSHLVKÖAEKEKT-FÖVNGGEÖFMVKDLS TGTSHLVKÖAEKEKT-FÖVNGGEÖFMVKDLS SWSGHARKÖNETAKS-YÖVNGGVÖYYIEGIN SWSGHARKÖNETAKS-YÖVNGGVÖYYIEGIN ERSEHFKPÖRDKDLA-YÖLNDGEÖFVIETLTG- MPTDHEEPÜGPSHKS-FÖLNGGLÖGVIPTIP	SVRNSDSEĞPLSHDG-YĞLHDGVĞMYIEALD—— AVVSHFNDÇPDSHTQ-FÖFH-GTĞRFLVQED—— KRKGHFSRQPKQYKH-YÇIK-GRĞRFVVAEQ—— RNRKKKNPĞNAEFQN-FÖIH-GEĞKYVEIR—— GLGKKRDPĞLRKYKD-FÖIH-GEĞKYVKEIR—— VAQVSITKĞSSDMNG-YÖLH-GQĞIYLVDMS—— VALKFSHPĞLEDHNS-YĞIN-GAĞAFHHELK——	:: #
Antagonists Argos Melanogasta	Agonists Lin-3	Vein Gurken Spitz Keren	NRG1_alpha NRG1_beta · NRG2_alpha NRG2_beta NRG3	EGF TGF_alpha Betacellulin Amphiregulin HB-EGF Epiregulin Epigen	Conserved cysteine

Figure 1

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WO 2005/017096

PCT/IL2004/000759



3/8

Sequence ID #

9 TGTSHLVKCAEKEKTFCVNGGECFMVKDLSNPSRYLCKCQPGFTGARCTENVPMKV TGTSHLVKCAEKEKTFCVNGGECFMVKDLSNPSRYLCKCPNEFTGDRCQNYVMASF SWSGHARKCNETAKSYCVNGGVCYYIEGINQLS—CKCPVGYTGDRCQQFAMVNF VAQVSITKCSSDMNGYCLH-GQCIYLVDMSQNY-CRCEVGYTGVRCEHFFLTVH 12 GLGKKRDPCLRKYKDFCIH-GECKYVKELRAPS---CICHPGYHGERCHGLSLPVE 11 MPTDHEEPCGPSHKSFCLNGGLCYVIPTIP-SP-FCRCVENYTGARCEEVFLPGS 6 SWSGHARKCNETAKSYCVNGGVCYYIEGINQLS-CKCPNGFFGQRCLEKLPLRL KRKGHFSRCPKQYKHYCIK-GRCRFVVAEQTPS--CVCDEGYIGARCERVDLFYL 9 SVRNSDSECPLSHDGYCLHDGVCMYIEALDKYA—CNCVVGYIGERCQYRDLKWW 7 ERSEHFKPCRDKDLAYCLNDGECFVIETLTGSHK-HCRCKEGYQGVRCDQFLPKTD AVVSHFNDCPDSHTQFCFH-GTCRFLVQEDKPA--CVCHSGYVGARCEHADLLAV RNRKKKNPCNAEFQNFCIH-GECKYIEHLEAVT---CKCQQEYFGERCGEKSMKTH VALKFSHPCLEDHNSYCIN-GACAFHHELKQAI—CRCFTGYTGQRCEHLTLTSY **Amphiregulin** NRG1_alpha VRG2_alpha VRG1_beta NRG2_beta Betacellulin IGF_alpha Epiregulin HB-EGF Epigen **JRG3** ARGA ARGA EGF

Figure 3

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	A	128	129	130	31	132	133	134
	ence	14 15 73, 1	16 17 74, 1	18 75, 1	9 6, 1	20 77, 1		
	Sequence	14 H (2		н г	47	2 7	21 78	22 79
	<pre></pre> <pre> <pre> </pre> <pre> <pre> </pre> <pre> <pre> </pre> <pre> <pre> </pre> <pre> <pre> </pre> <pre> </pre> <pre> </pre> <pre> </pre> <pre> <th>TGTSHLVKOAEKEKTFOUNGGEOFMUKDLSNPSRYLCKOPGFTGARCTENVPMKVO TGTSHLVKOAEKEKTFOUNGGEOFMUKDLSNPSRYLCKOPNEFTGDROONYVMASFY TGTSHLVKOAEKEKTFOUNGGEOFMUKDLSNPSRYLCK**</th><th>SWSGHARKONETAKSYCVNGGVCYYIEGINOESCKCPNGFFGORGLEKLPLRLY SWSGHARKONETAKSYCVNGGVCYYIEGINOLSCKCPVGYTGDRGOOFAWVNFY SWSGHARKONETAKSYCVNGGVCYYIEGINOLSCK</th><th>HERSEHFKPORDKDLAYOLNDGECFVIETLTGSHFKHOROKEGYOGVRODO-FLPKTD</th><th>MPTĎHÉEPGGPSHKSFOLNGGLOYVIPTIPSPRASSONTGARGEEVFLPGSS MPTĎHEEPGGPSHKSFOLNGGLOYVIPTIPSPRASSOR*</th><th>SVRNSDSECPLSHDGYGLHDGYGMYIEALDKYACNGVVGYIGERGOYRDLKWWE</th><th>TAVVSHENDCPDSHTOFCFH "GTCRFTVQEDKPA" "CVCHSGYVGARCEHADILAVV AVVSHENDCPDSHTOFCFH "GTCRFTVQEDKPA" "CV</th><th>KRKGHESROPKOYKHYOIK-GROREVVAEOTES TOOVODEGYIGARGERVDLFYLR</th></pre></pre></pre></pre></pre></pre>	TGTSHLVKOAEKEKTFOUNGGEOFMUKDLSNPSRYLCKOPGFTGARCTENVPMKVO TGTSHLVKOAEKEKTFOUNGGEOFMUKDLSNPSRYLCKOPNEFTGDROONYVMASFY TGTSHLVKOAEKEKTFOUNGGEOFMUKDLSNPSRYLCK**	SWSGHARKONETAKSYCVNGGVCYYIEGINOESCKCPNGFFGORGLEKLPLRLY SWSGHARKONETAKSYCVNGGVCYYIEGINOLSCKCPVGYTGDRGOOFAWVNFY SWSGHARKONETAKSYCVNGGVCYYIEGINOLSCK	HERSEHFKPORDKDLAYOLNDGECFVIETLTGSHFKHOROKEGYOGVRODO-FLPKTD	MPTĎHÉEPGGPSHKSFOLNGGLOYVIPTIPSPRASSONTGARGEEVFLPGSS MPTĎHEEPGGPSHKSFOLNGGLOYVIPTIPSPRASSOR*	SVRNSDSECPLSHDGYGLHDGYGMYIEALDKYACNGVVGYIGERGOYRDLKWWE	TAVVSHENDCPDSHTOFCFH "GTCRFTVQEDKPA" "CVCHSGYVGARCEHADILAVV AVVSHENDCPDSHTOFCFH "GTCRFTVQEDKPA" "CV	KRKGHESROPKOYKHYOIK-GROREVVAEOTES TOOVODEGYIGARGERVDLFYLR
	HUMAN	NRG1_alpha NRG1_beta Translated genomic locus	NRG2_alpha NRG2_beta Translated genomic locus	NRG3 Translated genomic locus	NRG4 Translated genomic locus	EGF Translated genomic locus	TGF_alpha Translated genomic locus	Betacellulin Translated genomic locus

Figure 4

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Amphiregulin Translated genomic locus	RNRKKKNPONAEFONFOIH-GEOKYIEHLEAVT-ROKGOOEYFGEROGEKSMKTHS RNRKKKNPONAEFONFOIH-GEOKYIEHLEAVT-ROK*	23 80, 135
HB-EGF Translated genomic locus	GLGKKRDPCLRKYKDFCIH-GECKYVKELRAPS CICHPGYHGERCHGLSLPVENGLGKKRDPCIRKYKDPCIH-GECKYVKELRAPS CICHPGYHGERCHGLSLPVEN	24 81, 136
Epiregulin Translated genomic locus	VAQVSITKCSSDWIGYCHHJGCGTYLVDWSQNYCRCEVGYTGVRCBHFFLTVHQ	25 82, 137
Epigen(Mouse) Trans. mouse genomic locus Trans. human genomic locus	VALKFSHPCHEDHNSYCIN-GACAFHHELKOATHEGERGFTGYTGORGEHLTLTSYAVALKESHPCHEDHNSYCIN-GACAFHHELKOATHEGERVALKFSHLCLEDHNSYCIN-GACAFHHELEKATHEGER.	26 83, 138

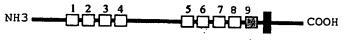
Figure 4 (continued)

6/8





ii) Epidermal Growth Factor



iii) Notch 1

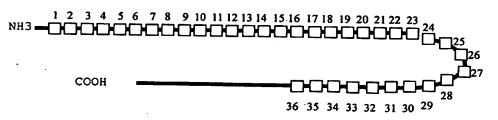


Figure 5A

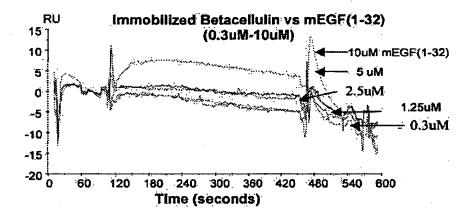
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i) TGF alpha EGF DOMAIN NUMBE 1. EGF_47_82	SequenceSEQUENCESEQUENCE	ID #
ii) EPIDERMAL	GROWTH FACTOR Sequence I	D #
EGF DOMAIN NUMBE	ocdactice T	D #
1. EGF 318 3		27
2. EGF 360 3	6 Nation Thice - Thice with the confidence with the confidence of	28
3. EGF 401 4		29
4. EGF 439-4	6 CSSINONGGEST ONGWEDGIR WSWEGDGERENDKONDEKSG	30
5. EGF_745 7	० <i>७७५७७५७७७० चेत्रावर्गकालस्य</i> न्द्रासम्बद्धसम्बद्धसम्बद्धाः	31
6. EGF_835_8		32
7. EGF_874_9	O GEMS-VENCEPPASSKGINUE-GENVCRGS-G-AXOGDGHHO	33
3. EGF_916_9	1 COLE-WIREGRANAS GRANAS GRANA	34
9. EGF_976_1		35
iii) Notch1	Sequen	ce I
GF DOMAIN NUMBE		
EGF_24_57	CSQPGETCLNGGKCEAANGTEACVCG-GAFVGPRC	· 36
EGF_63_98	CHEST TO THE THEORY MONITORING TO A PROPERTY OF THE PROPERTY O	37
EGF_106_138	GUT - NEGRNGGEGDHUMHUH HANKGRGF-EGWSGKSC	38
. EGF_144_175	@Ve)======== WeGVNGGo@=====#s5=134VeXe(o)(@s=E8)34@E6:4@	39
EGF_182_215	GCO	40
. EGF_222_254	SSESE - CONGGRORSIGDV - THE DOAGLERGFTGONC	41
. EGF_261_292	GEGUN	42
. EGF_299_332	SERSE - CONGENERATION - THANGRE PETTGONC GEORGE - CONGENERATION - THANGRE PETTGOYC GEORGE - THANGRE	43
EGF_339_370	EAS	44
0. EGF_376_409	ETSELECTED TO THE OFFICE OF THE CONTROL OF THE CONT	45
1. EGF_416_449	GSLGANPCEHAGKCINTLGSFECQCL-QGYTGPRC	46
2. EGF_456_487	CVS CHICANDANGLEDOIGE EFOCHOME PGYEGVHC	47
3. EGF_494_525	ZNS Stellingrol+dkanz-ziehoeege+egftghlc	48
4. EGF_532_563	@%9	49
5. EGF_570_600	GDPDP GING SCHOLDEWATTED FIGURE FRANKETHO	50
6. EGF_607_638	SOCIO	51
7. EGF_645_675	67/9	52
8. EGF_682_713	G.(G	53
9. EGF_720_750 0. EGF_757_788	ONS NECVICACED SIN HOW KCDCD-PGWSGTNC OLS NECVINGOICK DEMISSING COLOR RECESCION	54
1. EGF_795_826	G S TO THE MENT OF THE PROPERTY OF THE PROPERT	55
2. EGF_833_867	CAS : : : : : : : : : : : : : : : : : : :	56
3. EGF 874 905	CNP SPERNGGEOR-OSEDEYES-ESCUCETIAGAKGOTC	57
4. EGF 912 943	CVL	58
5. EGF 950 981	GRPNPCHNGGSCT-DGINTAFCDCL-PGFRGTFC	59
6. EGF 988 1019	CLE - ID	60
7. EGF 1026 105	GEESSCFNGGTCV-DGINSFTCLCP-PGFTGSYC	61
7. EGF_1026_105 8. EGF_1064_109	GDS	62
9. EGF_1004_109	SECURISM OF SECURI	63
9. EGF_1102_114 0. EGF_1150 118	EBYAAQROGVDVARLCQHGGLCV-DAGNTHHCRCQ-AGYTGSYC	64
1. EGF_1188_121	SEGONGATOT:DYIGGYSCKCV-AGYHGVNC	65
2. EGF_1226 126	CLS	66
2. EGF_1226_126 3. EGF 1272 130	AND MONTHS - SKALING PROVIDENCE: - CONCESSION - CONCESSION	67
4. EGF 1312 134	CLS	68
	GKGGFEGATC	69
5. EGF_1353_138	⊕ઃઃ વ્હામાલ માલવાલ કલાવા <mark>ર કર</mark> મેલાલા ત્વામાલ કરા	70
6. EGF_1392_142	on+====================================	71

Figure 5B



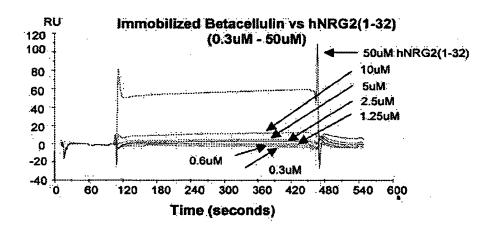


Figure 6